IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Engelhardt et al

Serial No. 08/479,997

Filed: June 7, 1995

Title: **OLIGO- AND POLYNUCLEOTIDES COMPRISING PHOSPHATE MOIETY LABELED NUCLEOTIDES**

Group Art Unit: 1631

Examiner: Ardin H. Marschel, Ph.D.

527 Madison Avenue, 9th Floor
New York, New York 10022
April 29, 2004

FILED VIA EXPRESS MAIL

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §§1.56 & 1.97-1.98

Dear Sirs:

Pursuant to the provisions of 37 C.F.R. §§1.97-1.98, and in full compliance with their duty of disclosure under 37 C.F.R. §1.56, Applicants, through their attorney, are bringing the following thirty-eight (38) documents to the attention of the U.S. Patent and Trademark Office and the Examiner handling their above-identified application:

EXPRESS MAIL CERTIFICATE

"Express Mail" Label No.: EV063169008US
Deposit Date: April 29, 2004

I hereby certify that this paper and the attachments herein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.110 on the date indicated above and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

APRIL 29 2004

Ronald C. Fedus — **Date**
Reg. No. 32,567

1. Adams, P.L., et al., Davidson's The Biochemistry of the Nucleic Acids, 8th Edition, Academic Press, New York, pp. 298-299 (1976) **[Exhibit 1]**;

2. Anderson, K.P., et al., U.S. Patent No. 5,591,720, filed August 14, 1991 **[Exhibit 2]**;

3. Baker, B.E., U.S. Patent No. 5,643,780, filed October 21, 1994 **[Exhibit 3]**;

4. Banker, M.J., et al., U.S. Patent No. 5,643,730, filed March 14, 1995 **[Exhibit 4]**;

5. Birch, G.G., et al., "Structural Functions and Taste in the Sugar Series; The Structural Basis of Bitterness in Sugar Analogues," J. of Food Science 41:1403-1407 (1976) **[Exhibit 5]**;

6. Chladek, S., et al., "Synthesis and Properties of Nucleoside 5'-Phosphoazidates Derived from Guanosine and Adenosine Nucleotides: Effect on Elongation Factors G and Tu Dependent Reactions," Biochemistry 16:4312-4319 (1977) **[Exhibit 6]**;

7. Cook, P.D., et al., U.S. Patent No. 5,614,617, filed July 1, 1991 **[Exhibit 7]**;

8. Crooke, S.T., et al., U.S. Patent No. 5,811,232, filed August 5, 1996 **[Exhibit 8]**;

9. Darlix, J.L., et al., "Analysis of Transcription *in Vitro* Using Purine Nucleotide Analogs," Biochemistry 10:1525-1531 (1971) **[Exhibit 9]**;

10. Darlix, J.L., et al., "Restriction of gene transcription by nucleotide analogs," Biochimie 56:703-710 (1974) **[Exhibit 10]**;

11. Ecker, D.J., et al., U.S. Patent No. 5,874,564, filed June 5, 1995 **[Exhibit 11]**;

12. Ecker, D.J., et al., U.S. Patent No. 5,736,924, filed June 27, 1991 **[Exhibit 12]**;

13. Ecker, D.J., U.S. Patent No. 5,591,600, filed March 18, 1992 **[Exhibit 13]**;

14. Eigen, M., et al., U.S. Patent No. 5,807,677, filed December 19, 1995 **[Exhibit 14]**;

15. Geider, K., "DNA Synthesis in Nucleotide-Permeable *Excherichia coli* Cells," Eur. J. Biochem. 27:554-563 (1972) **[Exhibit 15];**

16. Keppler, D.O.R., et al., "Uridylate trapping, induction of UTP deficiency, and stimulation of pyrimidine synthesis *de novo* by D-galactosone," Biochem J. 206:139-146 (1982) **[Exhibit 16];**

17. Kornberg, A., DNA Replication, W.H. Freeman & Company, San Francisco, Chapter 12, pp. 415-441, "Inhibitors of Replication" (1980) **[Exhibit 17];**

18. Kornberg, A., DNA Synthesis, W.H. Freeman & Company, San Francisco, Chapter 7, pp. 227-228, "Replication" (1974) **[Exhibit 18];**

19. Korytnyk, W., et al., "CMP and CMP-sugar analogs as inhibitors of sialic acid incorporation into glycoconjugates," Eur. J. Med. Chem. – Chimica Therapeutica 15:77-84 (1980) **[Exhibit 19];**

20. Langen, P., Antimetabolites of Nucleic Acid Metabolism, Gordon and Breach, New York, translated from German by Dr. Thomas A. Scott, pp. 143-187 (1975) **[Exhibit 20];**

21. Lartey, P.A., et al., "Preparation and Study of a Fluorescent Sugar Analog Competitive Inhibitor of Yeast Hexikinase," Preparative Biochemistry 9:85-95 (1979) **[Exhibit 21];**

22. Liu, et al., U.S. Patent No. 5,914,230, filed December 20, 1996 **[Exhibit 22];**

23. Marcus, F., "Inhibition of Fructose 1,6-Bisphosphatase by 9-B-D-Arabinofuranosyladenine 5'-Monophosphate," Cancer Research 36:1847 (1976) **[Exhibit 23];**

24. Martin, F.J., et al., U.S. Patent No. 5,891,468, filed October 10, 1997 **[Exhibit 24];**

25. Pagano, J.S., et al., U.S. Patent 5,242,906, filed April 22, 1991 **[Exhibit 25];**

26. Piperno, J.R., et al., "An ATP Stimulation of T4 DNA Polymerase Mediated via T4 Gene 44/62 and 45 Proteins," Journal of Biological Chemistry 253:5174-5179 (1978) **[Exhibit 26];**

27. Rahman, A., et al., U.S. Patent No. 5,665,710, filed December 10, 1993 **[Exhibit 27]**;

28. Reha-Krantz, L.J., et al., "Bacteriophage T4 DNA Polymerase Mutations That Confer Sensitivity to the PPi Analog Phosphonoacetic Acid," J. of Virology 67:60-66 (1993) **[Exhibit 28]**;

29. Roberts, K.R., et al., "Effects of 2-deoxy D-glucose and other sugar analogues on acid production from sugars by human dental plaque bacteria," Scandinavian Journal of Dental Research 88:201-209 (1980) **[Exhibit 29]**;

30. Ryser, H.J.P., et al., U.S. Patent No. 4,847,240, filed October 7, 1987 **[Exhibit 30]**;

31. Scheit, K.H., Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, New York, 280 pages (1980) **[Exhibit 31]**;

32. Schwartz, D.E., et al., U.S. Patent No. 5,212,059, filed January 9, 1989 **[Exhibit 32]**;

33. Simoncsits, A., et al., "A New Type of Nucleoside 5'-Triphosphate Analogue: P1-(Nucleoside 5"-) P1-Amino-Triphosphates," Tetrahedron Letters 44:3995-3998 (1976) **[Exhibit 33]**;

34. Stoeckler, J.D., et al., "Human Erythrocytic Purine Nucleoside Phosphorylase: Reaction with Sugar-Modified Nucleoside Substrates," Biochemistry 19:102-107 (1980) **[Exhibit 34]**;

35. Stridh, S., et al., "The Effect of Pyrophosphate Analogues on Influenza Virus RNA Polymerase and Influenza Virus Multiplication," Archives of Virology 61:245-250 (1979) **[Exhibit 35]**;

36. Usman, N., et al., U.S. Patent No. 5,652,094, filed January 31, 1992 **[Exhibit 36]**;

37. Wright, J.A., et al., U.S. Patent No. 5,998,383, filed August 1, 1997 **[Exhibit 37]**;

38. Yang, B.I-Y, et al., "Pyridoxal 5'-Phosphate and Analogs as Probes of Coenzyme-Protein Interaction," Methods of Enzymology 62:528-551 (1979) **[Exhibit 38]**.

The thirty-eight (38) foregoing references (numbers 1-38) have come to the attention of the Applicants' Attorney.

A completed Form PTO-1449 listing the 38 above-submitted documents is also attached hereto as Exhibit 39.

By this voluntary citation of art, Applicants and their attorney are requesting that the documents be made of record in the present application.

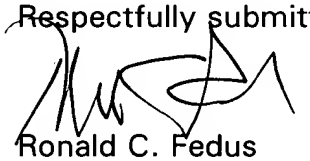
The above citation of documents is not a representation that these documents constitute a complete or exhaustive listing, nor that the above listing necessarily includes the closest or most relevant documents, nor are these documents necessarily a complete listing of all documents known to Applicants or their attorney. It is simply a voluntary citation of documents made in good faith, which is not intended to serve in any way as a substitute for the Examiner's own search.

In view of the general and specific features described and claimed in the present application, Applicants respectfully submit that the present invention is neither disclosed nor suggested by the documents referred to above and is thus patentably distinct thereover. Furthermore, Applicants do not believe, and do not submit, by the citation of these references, that these documents, either by themselves or in combination with other documents, render the invention *prima facie* obvious under the duty of disclosure rules.

Applicants respectfully request that the Examiner make the above-submitted documents of record in the instant application. Applicants further request that the Examiner consider these documents as any of them may relate to the instant application.

The fee under 37 C.F.R. §1.17(p) for filing this Information Disclosure Statement is $180.00. The Patent and Trademark Office is hereby authorized to charge the amount of this fee (and any other fees in connection with this IDS) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

Respectfully submitted,



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New York, New York 10022
Tel. (212) 583-0100

Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Atty. Docket No. ENZ-5(D6)(C2)	Serial No. 08/479,997
	Applicants: Engelhardt, et al	
	Filed: June 7, 1995	Group: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
		5 5 9 1 7 2 0	8/14/91	Anderson, et al			
		5 6 4 3 7 8 0	10/21/94	Baker, B.E.			
		5 6 4 3 7 3 0	3/14/95	Banker, et al			
		5 6 1 4 6 1 7	7/1/91	Cook, et al			
		5 8 1 1 2 3 2	8/5/96	Crooke, et al			
		5 8 7 4 5 6 4	6/5/95	Ecker, et al			
		5 7 3 6 9 2 4	6/27/91	Ecker, et al			
		5 5 9 1 6 0 0	3/18/92	Ecker, et al			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Adams, P.L., et al., Davidson's The Biochemistry of the Nucleic Acids, 8th Edition, Academic Press, New York, pp. 298-299 (1976)
		Birch, G.G., et al., "Structural Functions and Taste in the Sugar Series; The Structural Basis of Bitterness in Sugar Analogues," J. of Food Science 41:1403-1407 (1976)
		Chladek, S., et al., "Synthesis and Properties of Nucleoside 5'-Phosphoazidates Derived from Guanosine and Adenosine Nucleotides: Effect on Elongation Factors G and Tu Dependent Reactions," Biochemistry 16:4312-4319 (1977)
		Darlix, J.L., et al., "Analysis of Transcription *in Vitro* Using Purine Nucleotide Analogs," Biochemistry 10:1525-1531 (1971)
		Darlix, J.L., et al., "Restriction of gene transcription by nucleotide analogs," Biochimie 56:703-710 (1974)
		Geider, K., "DNA Synthesis in Nucleotide-Permeable *Excherichia coli* Cells," Eur. J. Biochem. 27:554-563 (1972)

EXAMINER	DATE CONSIDERED

***EXAMINER**: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. ENZ-5(D6)(C2)	Serial No. 08/479,997
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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
		5 8 0 7 6 7 7	12/19/95	Eigen, et al			
		5 9 1 4 2 3 0	12/20/96	Liu, et al			
		5 8 9 1 4 6 8	10/10/97	Martin, et al			
		5 2 4 2 9 0 6	4/22/91	Pagano, et al			
		5 6 6 5 7 1 0	12/10/93	Rahman, et al			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	TRANSLATION YES NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Keppler, D.O.R., et al., "Uridylate trapping, induction of UTP deficiency, and stimulation of pyrimidine synthesis *de novo* by D-galactosone," Biochem J. 206:139-146 (1982)
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		Korytnyk, W., et al., "CMP and CMP-sugar analogs as inhibitors of sialic acid incorporation into glycoconjugates," Eur. J. Med. Chem. – Chimica Therapeutica 15:77-84 (1980)
		Langen, P., Antimetabolites of Nucleic Acid Metabolism, Gordon and Breach, New York, translated from German by Dr. Thomas A. Scott, pp. 143-187 (1975)
		Lartey, P.A., et al., "Preparation and Study of a Fluorescent Sugar Analog Competitive Inhibitor of Yeast Hexikinase," Preparative Biochemistry 9:85-95 (1979)
		Marcus, F., "Inhibition of Fructose 1,6-Bisphosphatase by 9-B-D-Arabinofuranosyladenine 5'-Monophosphate," Cancer Research 36:1847 (1976)
		Piperno, J.R., et al., "An ATP Stimulation of T4 DNA Polymerase Mediated via T4 Gene 44/62 and 45 Proteins," Journal of Biological Chemistry 253:5174-5179 (1978)
		Reha-Krantz, L.J., et al., "Bacteriophage T4 DNA Polymerase Mutations That Confer Sensitivity to the PPi Analog Phosphonoacetic Acid," J. of Virology 67:60-66 (1993)

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	Filed: June 7, 1995	Group: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPRO-PRIATE
		4 8 4 7 2 4 0	10/7/87	Ryser, et al			
		5 2 1 2 0 5 9	1/9/89	Schwartz, et al			
		5 6 5 2 0 9 4	1/31/92	Usman, et al			
		5 9 9 8 3 8 3	8/1/97	Wright, et al			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	TRANS-LATION YES	NO

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		Roberts, K.R., et al., "Effects of 2-deoxy D-glucose and other sugar analogues on acid production from sugars by human dental plaque bacteria," Scandinavian Journal of Dental Research 88:201-209 (1980)
		Scheit, K.H., Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, New York, 280 pages (1980)
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		Stoeckler, J.D., et al., "Human Erythrocytic Purine Nucleoside Phosphorylase: Reaction with Sugar-Modified Nucleoside Substrates," Biochemistry 19:102-107 (1980)
		Stridh, S., et al., "The Effect of Pyrophosphate Analogues on Influenza Virus RNA Polymerase and Influenza Virus Multiplication," Archives of Virology 61:245-250 (1979)
		Yang, B.I-Y, et al., "Pyridoxal 5'-Phosphate and Analogs as Probes of Coenzyme-Protein Interaction," Methods of Enzymology 62:528-551 (1979)

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

JGW

04-30-04

1631

PTO/SB/17 (10-03)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 180.00

Complete if Known	
Application Number	08/479,997
Filing Date	June 7, 1995
First Named Inventor	Engelhardt
Examiner Name	Ardin H. Marschel, Ph.D.
Art Unit	1631
Attorney Docket No.	Enz-5(D6)(C2)

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 05-1135

Deposit Account Name: Enzo Biochem

The Director is authorized to: *(check all that apply)*

☑ Charge fee(s) indicated below ☑ Credit any overpayments

☑ Charge any additional fee(s) or any underpayment of fee(s)

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	180.00
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 180.00

SUBMITTED BY

(Complete *(if applicable)*)

Name *(Print/Type)*	Ronald C. Fedus	Registration No. *(Attorney/Agent)*	32,567	Telephone	212-583-0100
Signature				Date	April 29, 2004

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.